

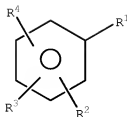
REMARKS

Claims 1-10, 12-13 and 15-60 are currently pending upon entry of this Letter to Patent and Trademark Office In Response to Office Action (hereinafter "Letter"). Claims 5, 12-13 and 26-60 have been withdrawn. No claims have been amended herein. Applicants respectfully request reconsideration and allowance of all pending claims.

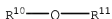
1. Rejection of Claims 1-4, 6-10, and 15-25 Under 35 U.S.C. § 103(a)

Reconsideration is requested of the rejection of claims 1-4, 6-10, and 15-25 under 35 U.S.C. § 103(a) as being unpatentable over any one of the following combinations: Lambert (J. Applied Microbiol.) and Syverson (U.S. 5,612,045) in view of Pacini, et al. (U.S. 3,393,678) and Cunningham (U.S. 4,318,404).

Claim 1 is directed to an exoprotein inhibitor for inhibiting the production of exoproteins from Gram positive bacteria in and around the vagina. The exoprotein inhibitor comprises a non-absorbent substrate for insertion into a vagina being selected from the group consisting of a non-absorbent incontinence device, a barrier birth control device, a tampon applicator, and a douche. The non-absorbent substrate has deposited thereon an effective amount of a first active ingredient and an effective amount of a second active ingredient. The first active ingredient has the general formula:



wherein  $R^1$  is  $-OR^6OH$ ;  $R^6$  is a divalent saturated or unsaturated aliphatic hydrocarbyl moiety;  $R^2$ ,  $R^3$ , and  $R^4$  are independently selected from the group consisting of H, OH, COOH, and  $-C(O)R^9$ ;  $R^9$  is hydrogen or a monovalent saturated or unsaturated aliphatic hydrocarbyl moiety. The second active ingredient has the general formula:



wherein  $R^{10}$  is a straight or branched alkyl or straight or branched alkenyl having from 8 to about 18 carbon atoms and  $R^{11}$  is selected from the group consisting of an alcohol, a polyalkoxylated sulfate salt and a polyalkoxylated sulfosuccinate salt. Both the first active ingredient and second active ingredient are effective in inhibiting the production of exoprotein from Gram positive bacteria.

Lambert discloses a method of examining the effect of inoculum size on the degree of inhibition observed with respect to inhibitor concentration. Specifically, the inoculum size dependencies of phenethyl alcohol, phenoxyethanol, p-chloro-m-cresol, trichloro-phenol, thymol, and dodecyltrimethylammonium bromide against *S. aureus* were analyzed. For some inhibitors examined, such as dodecyltrimethylammonium bromide ( $Cl_2QAC$ ), it was found that at lower inoculum levels, there was a greater biocidal effect, whereas at higher inoculum levels, there was a

greater degree of quenching of the biocide, causing the inhibitor to act more as a simple (sublethal) inhibitor. Lambert states that the method disclosed therein may be used to quantify the effect in the region between reversible and irreversible damage, or sublethal injury to cell death. Furthermore, Lambert states that the disclosed model suggests that on a molar basis, phenethyl alcohol is a better inhibitor than phenoxyethanol against *S. aureus*.

Significantly, however, as the Office recognizes on page 3 of the instant Office action, Lambert does not teach or suggest phenoxyethanol on a non-absorbent substrate. Further, Lambert does not teach or suggest an effective amount of a second active ingredient in combination with the first active ingredient deposited on a non-absorbent substrate. These are significant aspects of Applicants' claim 1.

Recognizing the deficiencies of Lambert, the Office cites the Syverson, Pacini, et al. and Cunningham references for combination with the Lambert reference in an attempt to arrive at each and every limitation of Applicants' claim 1.

Syverson is directed to **absorbent articles**, such as catamenial tampons, which include an effective amount of an ether compound to substantially inhibit the production of exotoxins by Gram positive bacteria. Specifically, the tampon contains an effective amount of the inhibiting ether compound to substantially inhibit the formation of TSST-1 when the tampon is exposed to *S. aureus* bacteria. The compositions can be prepared and applied in any suitable form, including aqueous solutions, lotions, balms, gels, salves, ointments, boluses, suppositories, and the like. The ether composition may additionally employ one

or more pharmaceutically acceptable and compatible carrier materials useful for the desired application.

Pacini, et al. disclose catamenial devices, such as tampons or vaginal inserts, and imparting upon them antibacterial qualities as well as physical lubricity that facilitates and lends comfort to their use. Specifically, Pacini, et al. disclose that polymetallic pectinates can be made into films or their dispersions may be sprayed on or applied to materials intended for vaginal tamponing. The coating is used to better facilitate the insertion into the vaginal vault. The advantages of the coating can include: (1) development of a gelatinous film that facilitates the introduction of the tampon or applicator; (2) liberation from the gel of galacturonic acid resulting from the destructive hydrolysis of the pectin; and, (3) liberation for diffusion over the mucosal surfaces of the vaginal vault of metal pectinates, which exert bactericidal and/or protozoicidal effectiveness.

Cunningham discloses an applicator for a tampon having a convolution so as to double the applicator upon itself to form parallel walls with the convolution therebetween. The applicator comprises a flexible sleeve about the tampon and overlaps a portion of the forward end of the tampon. Suitable materials for the sleeve include polyethylene or polypropylene. The sleeve may be coated with an appropriate lubricant.

In order for the Office to show a *prima facie* case of obviousness, M.P.E.P. § 2142 requires a clear articulation of the reasons why the claimed invention would have been obvious. Specifically, the Supreme Court in *KSR International Co. v. Teleflex Inc.*, 550 U.S. 398, 82 USPQ2d 1385, 1396 (2007) noted

that the burden lies initially with the Office to provide an explicit analysis supporting a rejection under 35 U.S.C. 103. "[R]ejections on obviousness cannot be sustained with mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." The Court in KSR International further identified a number of rationales to support a conclusion of obviousness which are consistent with the proper "functional approach" to the determination of obviousness as laid down in *Graham v. John Deere Co.* (383 U.S. 1, 148 USPQ 459 (1966)). Specifically, as previously required by the TSM (teaching, suggestion, motivation) approach to obviousness, one exemplary rationale indicated requires some teaching, suggestion, or motivation in the prior art reference that would have led one of ordinary skill to modify the prior art reference to arrive at the claimed invention. Specifically, to reject a claim based on this rationale, the Office must articulate the following: (1) a finding that there was some teaching, suggestion, or motivation, either in the reference itself or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings to arrive at each and every limitation of the claimed invention; (2) a finding that there was reasonable expectation of success; and (3) whatever additional findings based on the *Graham* factual inquiries may be necessary, in view of the facts of the case under consideration, to explain a conclusion of obviousness. The Office has failed to meet its burden under number (1) above, as there is no apparent reason for one skilled in the art to modify and/or combine the references to arrive at

each and every limitation. It simply would not have been obvious to one skilled in the art to arrive at Applicants' claimed combinations.

Specifically, nowhere in the cited references (or in the knowledge available to one skilled in the art) is there an apparent reason to combine the references to arrive at each and every limitation of Applicants' claim 1. As recognized by the Supreme Court in KSR International Co. v. Teleflex, Inc., while an obviousness determination is not a rigid formula, the TSM (teaching, suggestion, motivation) test captures a helpful insight: "A patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art. Although common sense directs [caution as to] a patent application that claims as innovation the combination of two known [elements] according to their established functions, it can be important to identify a reason that would have prompted a person of ordinary skill in the [art] to combine the elements in the way the claimed new invention does."<sup>1</sup>

Initially, as noted above, Lambert fails to teach or suggest depositing a second active ingredient onto a non-absorbent substrate. On page 4 of the current Office action, the Office states that it would have been obvious to combine Lambert and Syverson because both references are effective against *S. aureus* and suggest employing compounds for inhibiting toxic shock syndrome. Applicants respectfully disagree.

Specifically, why would one having ordinary skill in the art be motivated to add a second active ingredient to Lambert

when Lambert already teaches that phenoxyethanol has sufficient inhibitory characteristics?

In the Response to Arguments section of the instant Office action, the Office states that Lambert discloses phenoxyethanol with a second active ingredient because "Lambert teaches different compounds and their effect on the reversible and irreversible damage to various inoculum levels of *S. aureus*." Applicants respectfully disagree. Although Lambert discloses six compounds in their study, Lambert does not suggest combining the compounds to form a first and second active ingredient. That is, Lambert looks at the inhibitory effects of the compounds individually, and not in combination. Furthermore, although Lambert studied the inoculum size dependencies of various compounds, Lambert does not teach or suggest combining the various compounds with a second active ingredient, much less teach or suggest combining the compounds with the second active ingredient of Syverson or Applicants' claim 1.

Moreover, even if one having ordinary skill in the art decided to combine the phenoxyethanol of Lambert with the active ingredient of Syverson (which, as noted above, Applicants respectfully submit one would not), there still is no reason to deposit the compounds on a non-absorbent substrate, as is required in Applicants' claim 1. In this regard, in the current Office action, the Office states that it would have been obvious to combine Lambert and Syverson onto a non-absorbent substrate because Syverson teaches that the tampon may or may not have an applicator, Pacini, et al. teach that antimicrobial compounds may be employed in the tampon fabric itself or in the enclosure

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<sup>1</sup> 2007 WL at 5.

that holds tampons, and/or, Cunningham teaches an applicator with a non-absorbent material. Applicants respectfully assert that such a combination simply could not, and would not, be made.

Specifically, Applicants submit that there is no reason to combine Lambert and Syverson with Pacini, et al., because nowhere in Pacini, et al. is the inhibition of exoproteins ever discussed. That is, Pacini, et al. merely disclose that polymetallic pectinates or their dispersions can be placed onto a tampon. This is completely different, however, then depositing the first and second active ingredient onto a non-absorbent substrate in order to inhibit the production of exoproteins from Gram positive bacteria, as is required by Applicants' claim 1. In particular, why would one having ordinary skill in the art, when looking to inhibit the production of exoproteins from Gram positive bacteria, such as Lambert and Syverson are directed at, look to a reference, such as Pacini, et al., that is directed toward a coating of polymetallic pectinates, which are completely separate and distinct compounds from those of Applicants' claim 1 (or as taught in Lambert and Syverson)? Particularly, when nowhere in Pacini, et al. are the first active ingredients of Applicants' claimed invention (such as the phenoxyethanol of Lambert) or the second active ingredients of Applicants' claimed invention (such as the ethers of Syverson) taught or suggested. Furthermore, nowhere in Pacini are exoproteins from Gram positive bacteria even mentioned, or the importance of their inhibition thereof? It simply cannot be stated that it would be obvious to do so. This is particularly true in the instant case, where

Syversen already discloses that depositing an active ingredient on an absorbent tampon can inhibit exoprotein production from Gram bacteria. The Office has simply not proffered any evidence why it would be obvious to combine the cited references.

Further, there is no reason to combine Lambert, Syversen and Pacini, et al. with Cunningham in order to arrive at the exoprotein inhibitor or Applicants' claim 1. Initially, Applicants note that, as recognized by the Office, neither Lambert, Syversen nor Pacini, et al. teach or suggest non-absorbent tampon applicators with active ingredients deposited thereupon. As such, why would one having ordinary skill in the art look to combine the cited references with the non-absorbent applicator of Cunningham? Particularly, why would one having ordinary skill in the art look to modify Syversen (which, already provides for an effective means of inhibiting exproteins with an absorbent article) and/or Pacini, et al. (which, already provides for an effective means of placing an antimicrobial substance on an absorbent tampon applicator) with the non-absorbent applicator of Cunningham? Moreover, nowhere does Cunningham ever mention depositing any antimicrobial/antibacterial substance on its non-absorbent applicator, or the importance thereof. Why, then, would one having ordinary skill in the art, look to combine Cunningham with the cited references to arrive at the exoprotein inhibitor comprising the non-absorbent substrate of Applicants' claim 1? It simply does not follow that it would be obvious to do so. As the cited references: (1) already provide for a means of applying antimicrobial substances to tampon absorbent articles; (2) none of Lambert, Syversen or Pacini, et al. disclose or

suggest applying the antimicrobial substances to a non-absorbent article; and, (3) Cunningham does not disclose or suggest depositing any antimicrobial substance onto its non-absorbent applicator, there is simply no reason to modify the cited references to include the non-absorbent applicator of Cunningham.

Moreover, as discussed in the previous response, the common sense of one ordinarily skilled in the art would not have provided a reason to combine or modify the cited references to arrive at Applicants' exoprotein inhibitor comprising a first active ingredient and a second active ingredient having the structures as required in claim 1 deposited on a non-absorbent substrate. Specifically, as discussed previously, absorbent and non-absorbent substrates have inherently different properties, and there is nothing in any of the cited references to suggest that the compounds of any of the cited references would be effective if used with a non-absorbent substrate. For instance, in the instant application, paragraph [0014] provides an example of how a non-absorbent substrate (e.g., tampon applicator) differs from an absorbent article such as a tampon. Specifically, the non-absorbent tampon applicator, which may have deposited thereon the claimed first and second active ingredients, houses the absorbent tampon. When the applicator is introduced into a woman's vaginal cavity, the first and second active ingredients are transferred from the non-absorbent applicator onto the wall of the vagina. The non-absorbent applicator is then removed from the cavity while the absorbent tampon remains in the cavity to absorb fluids. Thus, it would not be obvious to one having ordinary skill in the art to modify

the teachings of the cited references to arrive at the non-absorbent substrates of Applicants' claim 1.

Based on the foregoing, it appears that the Office has used impermissible hindsight and reconstruction (using the Applicants' claimed invention as a blueprint) for arriving at such a combination/modification. The Federal Circuit has consistently warned against this type of analysis.

Specifically, in order to arrive at the exoprotein inhibitor of Applicants' claim 1, one having ordinary skill in the art would first have to combine the phenoxyethanol of Lambert, which teaches that phenoxyethanol alone is sufficient to inhibit *S. aureus* and, further, does not disclose or suggest combining phenoxyethanol with a second active ingredient, specifically, with the ether compounds of Syverson, which do not disclose or suggest combining the ether compounds with another ingredient. Then, one would have to select Pacini, et al., which nowhere discusses exoprotein inhibitors for inhibiting the production of exoproteins from Gram positive bacteria. Finally, one having ordinary skill in the art would then have to combine the cited references with the non-absorbent applicator of Cunningham, when none of the aforementioned references disclose or suggest depositing antimicrobial/antibacterial compounds onto a non-absorbent tampon applicator, and, when nowhere in Cunningham is it ever discussed to apply antibacterial/antimicrobial substances on the non-absorbent applicators disclosed therein. As noted above, one would have to do this without using Applicants' disclosure as a blueprint. Applicants respectfully submit that it cannot be stated that it would be obvious to do so.

For the reasons set forth above, it is not foreseeable or predictable that one skilled in the art would simply combine the phenoxyethanol of Lambert and the ether compound of Syverson with the applicator of Pacini, et al. and the non-absorbent applicator of Cunningham to arrive at the specific exoprotein inhibitor of Applicants' claim 1. As such, Applicants respectfully assert that the motivation suggested by the Office for combining the cited references does not meet the requirements as set forth in the Office's guidelines for evaluating an obviousness rejection.

As there is no apparent reason for one skilled in the art to combine the cited references to arrive at each and every limitation of Applicants' claim 1, claim 1 is patentable over the Lambert, Syverson, Pacini, et al. and Cunningham references.

Claims 2-4, 6-10 and 15-25 depend from claim 1 and are thus patentable over the cited references for the same reasons set forth above for claim 1, as well as for the additional limitations they require.

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**CONCLUSION**

In view of the above, Applicants respectfully request favorable reconsideration and allowance of all pending claims. The Commissioner is hereby authorized to charge any fee deficiency in connection with this Response to Office Action to Deposit Account Number 01-2384.

Respectfully Submitted,

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